PSJ17 Exh 82

FAX COVER SHEET

DIVISION OF DRUG MARKETING, ADVERTISING, AND COMMUNICATIONS
CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

Date: March 26, 2009

T : **Carole S. Marchione**
Senior Director and Group Leader
Regulatory Affairs
Cephalon, Inc.

Phone: (610) 738-6237 **Fax:** (610) 738-6642

From: Michael Sauers
Regulatory Review Officer

Comments: If you have any questions, please contact me at (301) 796-1200.
Thank you.

No. of Pages without coversheet: 4

Phone: 301-796-1200

Fax: 301-847-8444

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Carole S. Marchione
Senior Director and Group Leader, Regulatory Affairs
Cephalon, Inc.
41 Moores Road, PO Box 4011
Frazer, PA 19355

RE: NDA #21-947 FENTORA (fentanyl buccal tablet)
NDA #22-249 TREANDA (bendamustine hydrochloride) for Injection, for intravenous Infusion
MACMIS ID #17321

Dear Ms. Marchione:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed Cephalon, Inc.'s (Cephalon) sponsored links on internet search engines (e.g., Google.com) for the following products: FENTORA (fentanyl buccal tablets) (Fentora), and TREANDA (bendamustine hydrochloride) for Injection (Treanda). The sponsored links ar misleading because they make representations and/or suggestions about the efficacy of Fentora and Treanda, but fail to communicate **any** risk information associated with the use of these drugs. In addition, the sponsored link for Fentora inadequately communicates the drug's indication. Furthermore, all of the sponsored links fail to use the required established name. Thus, the sponsored links misbrand the drugs in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

Background

Fentora

According to its FDA-approved product labeling (PI), "*FENTORA* is indicated only for the management of breakthrough pain in patients with cancer who are **already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain** . . . . [emphasis in original]

This product **must not** be used in opioid non-tolerant patients because life-threatening hypoventilation and death could occur at any dose in patients not on a chronic regimen of opioids" (underline emphasis added).

Fentora is associated with a number of risks, as reflected in the Boxed Warning, Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Treanda
According to its FDA-approved PI, Treanda is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL). Efficacy relative to first line therapies other than chlorambucil has not been established.

Treanda is associated with a number of risks, as reflected in the Contraindications, Warnings and Precautions, and Adverse Reactions sections of its PI.

Omission of Risk Information

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims:

- FENTORA Information
  www.FENTORA.com Learn about treating breakthrough pain in patients with cancer.
- TREANDA Now Available
  www.TREANDA.com Learn more about a unique therapy for CLL patients.

These sponsored links make representations and/or suggestions about the efficacy of Fentora and Treanda, respectively, but fail to communicate **any** risk information. This omission of risk information is particularly concerning as one of the products, Fentora, has a Boxed Warning. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any claims made in that part.

By omitting the most serious and frequently occurring risks associated with the drugs promoted in the links above, the sponsored links misleadingly suggest that Fentora and Treanda are safer than has been demonstrated. We note that these sponsored links contain a link to the products' websites. However, this is insufficient to mitigate the misleading omission of risk information from these promotional materials.

Inadequate Communication of Indication

Th sponsored link for Fentora provides a very brief statement about what the drug is for; however, this statement is incomplete and misleading, suggesting that Fentora is useful in a broader range of conditions or patients than has been demonstrated by substantial evidence or substantial clinical experience. Specifically, the sponsored link misleadingly broadens the indication for Fentora by implying that any patient with cancer who requires treatment for breakthrough pain is a candidate for Fentora therapy ("Learn about treating breakthrough pain in patients with cancer"), when this is not the case. Rather, Fentora is only indicated for the management of breakthrough pain in cancer patients who are **already receiving and**

who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. The misleading suggestion conveyed by the sponsored link that Fentora is appropriate for all cancer patients with breakthrough pain is especially concerning given that F ntora **must not** be used in opioid non-tolerant patients because life-threatening hypoventilation and death could occur at any dose in patients not on a chronic regimen of opioids.

Failure to Use Required Established Name

None of the sponsored links present the full established name of the drugs being promoted, despite the requirement to do so. *See* 21 CFR 201.10(g)(1) & 202.1(b)(1).

Conclusions and Requested Action

For the reasons discussed above, the sponsored links misbrand Fentora and Treanda in violation of the Act and FDA regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

DDMAC requests that Cephalon immediately cease the dissemination of violative promotional materials for Fentora and Treanda, such as those described above. Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission dat) in use for these drugs as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials. Finally, we encourage you to review your promotional materials for the other prescription drug products that Cephalon promotes in the United States and to discontinue or revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondences regarding this matter, please refer to MACMIS #17321 in addition to the NDA numbers. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Fentora and Treanda comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Michael Sauers
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Michael A Sauers
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